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Sparteine, a Ligand for Magnesium in Organometallics: Nuclear Magnetic Resonance Studies of Exchange

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Summary The existence and structure, (I), of strong sparteine R_2Mg complexes, which undergo inversion, carbon–magnesium bond exchange, and magnesium ligand exchange unusually slowly, have been established by n.m.r. studies.

Sparteine has been used since 1870 as a drug for various muscle disorders, especially those involving heart malfunction and irregularities during labour.[1] We now present results from n.m.r. studies which show that sparteine is an exceptionally good ligand for magnesium and that under some circumstances magnesium–sparteine ligand exchange is slow on the n.m.r. time scale.

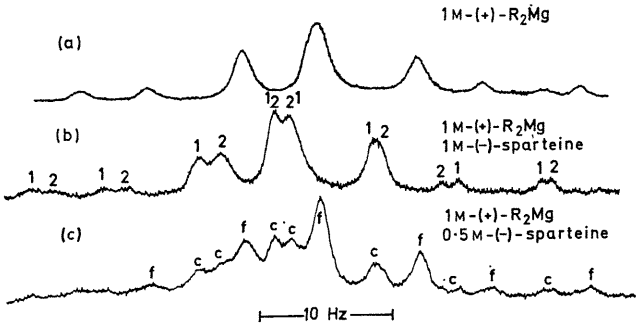


Figure *N.m.r. spectra, 60 MHz, 30°, $-CH_2Mg$ of bis-(2-methylbutyl)magnesium with and without sparteine, solvent ether.*

The n.m.r. absorption for the CH_2Mg hydrogens of bis-(2-methylbutyl)magnesium, R_2Mg, in ether, Figure (a), consists of the AB part of a single ABX system. With increasing temperature, above 50°, the AB shift becomes progressively averaged due to the increasing rate of inversion and it is possible to calculate the inversion rate from the CH_2Mg proton line-shape.[2]

That only one resonance for the 2-methylbutyl group is observed above −70° indicates that fast carbon–magnesium bond exchange averages the shifts among the several different species known to be present in ether solutions of dialkylmagnesium compounds.[3]

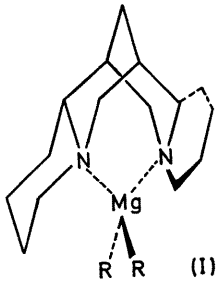
From n.m.r. studies of dialkylmagnesium compounds in mixtures of ethers and tertiary amines it is found that, although both ether and amine magnesium complexes are present, fast magnesium ligand exchange averages the shifts among the different species,[2] above −70°.

Thus, in the case of R_2Mg in ether from −70° upwards, both carbon–magnesium bond exchange and magnesium–ether co-ordination exchange are fast on the n.m.r. time scale ($k_1 < 10^5\ s^{-1}$), while above 50° inversion rates can be measured with n.m.r. techniques.

In contrast to the above results, when R_2Mg is mixed with free sparteine, both 1M, the n.m.r. absorption for $-CH_2Mg$ consists of two AB parts of different ABX systems which are labelled 1 and 2 in Figure (b). This spectrum does not change with temperature between −30 and +80°. However, with 1M-(+)-R_2Mg and 0·5 M-sparteine the n.m.r. spectrum, Figure (c), shows AB parts of three different ABX systems; two coincide with those for the equimolar mixture (peaks labelled c), the third is identical to that for pure R_2Mg in ether (peaks labelled f). When these experiments were undertaken with (±)-R_2Mg the CH_2–Mg resonance contained complicated overlapping patterns.

Comparison of Figures (b) and (c) shows that (b) represents a 1:1 complex of R_2Mg with sparteine. In this complex the alkyl groups are in different environments with different sets of chemical shifts. That the spectrum of (±)-R_2Mg with sparteine is so complex can only mean that

several diastereomers are present and that exchange among them is slow on the n.m.r. time scale. This situation persists up to 90°. Beyond this temperature boiling in the sample tube destroys instrumental resolution.



(I)

The observations reported here are best explained if the R_2Mg sparteine complex is represented by (I). In this caged structure the co-ordination of both nitrogens to the same magnesium is responsible for the *cisoid* configuration. This differs from the *transoid* structure determined for free sparteine by n.m.r. spectroscopy.[4] Furthermore, the skewed nature of the rings in (I) accounts for the different magnetic environments of the alkyl groups on magnesium.

The temperature independence of the n.m.r. spectrum of pure (I) indicates that carbon–magnesium bond exchange, magnesium–nitrogen co-ordination exchange, and inversion are all slow on the n.m.r. time scale. This result is in distinct contrast to the fast exchange processes usually detected when organomagnesium compounds complex with ethers and tertiary amines.

When mixtures of (I) with free R_2Mg in ether are warmed above 60° the resonances for the different species present coalesce. Under these conditions the exchange and inversion process described above are on the n.m.r. time scale. Hence the line-shapes are being used to investigate the mechanisms of the different processes.

Similar results to those presented here have been obtained with dineopentylmagnesium, ditolylmagnesium, diallylmagnesium, and butyl-lithium.

From our results it is evident that sparteine is a good ligand for magnesium. While magnesium sulphate inhibits labour in both animal and human systems sparteine acts as a stimulant. It is possible that sparteine acts physiologically by complexing magnesium and possibly other metal ions.

It is known that hyperkalaemia induced by nicotine is suppressed by sparteine,[6] and that sparteine increases the amount of KCl required to induce fibrillation.[7] However, there is no evidence on how sparteine together with magnesium salt effects muscle contraction.

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